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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,193	06/20/2005	Dulce Elena Casarini	0002150USU/2417	2762

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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,193	CASARINI ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/20/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, step (b), "the previous established standards" lacks antecedent basis.

With respect to claim 1, step (b), "the hypertensive genetic markers" lacks antecedent basis.

With respect to claim 1, step (b), "(for example, fresh or concentrated)" the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

With respect to claim 1, step (b), "the ACE recombinant enzyme" lacks antecedent basis.

With respect to claim 1, step (c), "predisposed persons" it is not clear whether this step corresponds to step (a) "living organisms" for consistency.

With respect to claim 3, last line, it is not clear what "[90 kDa and 65kDa]" with respect to the following 190 kDa, 90kDa and 65 kDa. In particularly, it is confusing about the usage of "[ ]".

With respect to claim 5, line 3, it is confusing and vague with the wording "it is detected". It is not clear what does applicant means "it is detected".

With respect to claim 8, line 1, "the potential of 90 kDa" lacks antecedent basis.

With respect to claim 8, step (c), it is not clear what "(n= 21)" stands for. Similarly, throughout the rest of the claims, a lot of the same problem occurs. Applicant needs to clarify.

With respect to claim 8, step (c), line 3, " with as well as" is confusing since the previous isoforms already include 90 and 65 kDa, it is not clear whether applicant intends to recite only two isoforms, i.e. 90 kDa and 65 kDa. It is suggested that applicant avoids using "as well as", rather using "and". It is also confusing about the recitation "with the ACE activity (170 kDa and 65 kDa), from isoform (170, 90 and 65 kDa)". What is the relationship of the "90 kDa" playing here? It is not consistent with the previous 2 kDa markers if observing from the three markers. Applicant needs to clarify.

Claims 14-16 and 22 provides for the **use** of genetic marker, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.
Claims 14-16 and 22 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

With respect to claim 17, line 3, it is not clear about the term "carriers" in relation to the context of the recited preamble. Are these "carriers" mean persons? Again, line 6, the

wording "it is detected" is also confusing in relation to the recited method. Furthermore, there is no specific active step in this claim, applicant merely recites "wherein".

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 2, 4-7, 13-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Casarini et al. (Intl. J. Biochem Cell Biology 2001 Vol. 33, page 75-85; note the publication date is Jan 2001 online).

Casarini et al. teach a method of identifying and quantifying of isoforms of angiotensin I converting enzymes (ACE) in biological fluids, e.g. urine (See Abstract). Casarini et al. teach collecting an aliquot of concentrated urine and submit the samples to separation and Western blot analysis (See page 76 Method and Figure 5 for Western blot analysis). Casarini et al. identify different hypertensive genetic makers, such as 65 kDa, 90 kDa and 190 kDa (See Abstract; page 79, right column first paragraph; Figure 5) where the 190 kDa and 65 kDa are in normal individuals, and the maker of 90 kDa appears in hypertension people. Supra.

With respect to claims 2, 18 and 21, Casarini et al. teach that the 90 kDa is a hypertension marker and a prognostic agent for hypersension. Surpa.

With respect to claims 4 and 19, Casarini et al. teach collecting urine samples for analysis. Surpa.

With respect to claims 5, 7, Casarini et al. also show that the two peaks eluted by chromatography, corresponding to 65 kDa and 190 kDa (See page 83, right column, third paragraph; also the cited reference 19).

With respect to claim 6, Casarini et al. also teach using ion exchange chromatograph (See page 77, left column, second paragraph).

With respect to claims 13-14, Casarini et al. teach that the 90 kDa marker can a prognostic tool for hypertension marker for (See Results and Discussion; Abstract).

With respect to claim 16, Casarini et al. teach the target organ is the kidney (See Method).

With respect to claim 17, Casarini et al. teach using the three 190, 90 and 65 kDa markers to evaluate the hypertension. Supra.

With respect to claim

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hattori et al. (Hypertension 2000 Vol. 35, page 1284-1290 ; applicant submitted IDS informaiton).

Hattori et al. teach a method of identifying and quantifying of isoforms of angiotensin I converting enzymes (ACE) in tissues, cells and biological fluids, e.g. urine (See Abstract). Hattori et al. teach collecting an aliquot of concentrated urine with Tris-HCL 50 mM buffer, pH 8.0, submit to gel filtration in AccA-34 column equilibrated with Tris-HCL 50 mM buffer, concentrated NaCl 150 m, pH 8.0 (See Method, page 1285) and collect urine samples determining protein amount at A280 nm and measuring angiotensin I activity by using appropriate substrates, such as Hipuril-L-His-L-Leu and Z-Phe-His-Leu (See cited reference 22 by Friedland et al.). Hattori et al. identify different hypertensive genetic makers, 170 kDa, 90 kDa and 65 kDa (See Abstract). Hattori et al. disclose that the 90 kDa is detected in the mild hypertension patients (See Abstract). With respect to the "(n=21) or (n=13)", it is believed referring to the sample of size (See above 35 USC 112, 2nd paragraph rejection). It is noted that the sample size Hattori et al. is slightly different from the current invention, i.e. n=15 vs. n= 13 or 21.

Nevertheless, it would have been obvious to one ordinary skill in the art at the time the invention was made to use slightly different size of sample to observe the similar detected markers, i.e. 170, 90 and 65 kDa. The slightly size of samples may reflect different intensity, however, the marker itself would remain the same. This would be obvious to one ordinary skill in the art.

With respect to claims 9 and 11, the marker of 170, 90 and 65 kDa are used to detect in the normotensive and hyepertensive parents (See Method and Materials).

With respect to claim 10, three markers, 170, 90 and 65 kDa are used to detect and Hattori et al. teach that the 90 kDa detected in hypertensive parents. Surpa.

With respect to claim 12, the 90 kDa is a marker for hypertension and can be served as a prognostic agent for hypertension. Surpa.

8. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Casarini et al. and further in view of Karst et al. (US 20030062475).

Casarini et al. teach using chromatography AcA34 resin and C-18 column for separation of protein samples, and subsequent analysis by Western blot and identify 190, 90 and 65 kDa isoforms of ACE (See page 77-78). However, Casarini et al. do not explicitly teach using mass spectrometer for separation.

Karst et al. teach that combining both chromatography and mass spectrometer provides advantage of efficient separation of protein complexes from the sample (See Section 0002).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided Casarini et al. with the mass spectrometer in combination with the chromatography column as taught by Karst et al. in order to achieve separation of protein complex samples more efficiently.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jacob Cheu
Examiner
Art Unit 1641

September 10, 2007

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